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Bioavailability of Arsenic in Soil and House Dust Impacted by Smelter Activities Following Oral Administration in Cynomolgus Monkeys

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This study was conducted to determine the extent of arsenic (As) absorption from soil and house dust impacted by smelter activities near Anaconda, Montana. Female cynomolgus monkeys were given a single oral administration via gelatin capsules of soil (0.62 mg As/kg body wt) or house dust (0.26 mg As/kg body wt), or soluble sodium arsenate by the gavage or intravenous route of administration (0.62 mg As/kg body wt) in a crossover design with a minimum washout period of 14 days. Urine, feces, and cage rinse were collected at 24-hr intervals for 168 hr. Blood was collected at specified time points and area under the curves (AUCs) was determined. Arsenic concentrations for the first 120 hr, representing elimination of greater than 94% of the total administered dose for the three oral treatment groups, were <0.021 to 4.68 μg/ml for the urine and <0.24 to 31.1 μg/g for the feces. In general, peak concentrations of As in the urine and feces were obtained during the collection intervals of 0–24 and 24–72 hr, respectively. The main pathway for excretion of As for the intravenous and gavage groups was in the urine, whereas for the soil and dust groups, it was in the feces. Mean absolute percentage bioavailability values based on urinary excretion data were 68, 19, and 14% for the gavage, house dust, and soil treatments, respectively, after normalization of the intravenous As recovery data to 100%. Corresponding absolute bioavailability values based on blood were 91, 10, and 11%. The bioavailability of soil and house dust As relative to soluble As (by gavage) was between 10 and 30%, depending upon whether urinary or blood values were used. These findings suggest that risks associated with the ingestion of As in soil or dust will be reduced compared to ingestion of comparable quantities of As in drinking water. © 1995 Society of Toxicology.

Arsenic (As) concentrations are elevated locally in soils at many sites of former mining and smelting activities around the world. Even more widespread contamination has occurred due to the use of arsenical pesticides and defoliants (Chaney and Ryan, in press). Orchards and cotton and potato fields have been particularly contaminated. It has been estimated that, in the United States alone, 100,000 to 1,000,000 hectares of current and former agricultural land contain soil As concentrations of 200 μg/g or more while tens of millions of hectares contain arsenic residues in the range of 20 to 30 μg/g (R. L. Chaney, personal communication). Because As carcinogenicity has been estimated by the U.S. EPA from studies of Taiwanese populations (Tseng, 1977; Tseng *et al.*, 1968) with As in drinking water (soluble As), it is important to assess As bioavailability from soil, relative to soluble As, in order to accurately assess risks from ingestion of soil As.

Such an assessment depends, in part, on a determination of As bioavailability in soil relative to water. Bioavailability is defined as the extent to which the chemical is absorbed into the systemic circulation and distributed to the target organs. In a previous experiment using New Zealand White rabbits (Freeman *et al.*, 1993), urinary excretion data revealed that the absolute bioavailability of As in soil from a former copper smelter site was less than 30%. Arsenic in the soil was approximately twofold less bioavailable than arsenic in solution, indicating that soil As was in a less readily available form. However, due to concerns about physiological dissimilarities between rabbits and humans, particularly the occurrence of coprophagy in rabbits, it was decided that soil As bioavailability should be tested in a second animal model. The monkey was subsequently chosen as an animal model with more physiological and anatomical similarity to humans.

The current study was designed to characterize the extent of As absorption from residential soil and house dust impacted by past smelter emissions. Blood As concentrations and urinary excretion of As was assessed in cynomolgus monkeys sequentially receiving intravenous sodium arsenate solution and three different oral treatments: soil in capsules, house dust in capsules, and sodium arsenate solution administered by gavage.

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METHODS

Materials

The composite soil (9 residences) and house dust (4 residences) samples administered to the monkeys were collected from residences in Anaconda, Montana. Disodium arsenate heptahydrate ($Na_2HAsO_4 \cdot 7H_2O$) obtained from Aldrich Chemical Co. (Milwaukee, WI) was used to administer the appropriate doses of As to the intravenous and gavage study group animals.

Test Substance Composition

Moisture content was determined by weight loss after drying at 105°C for 2 hr. Percentage organic matter in the test soil was estimated from loss-on-ignition at 430°C until constant weight or after heating for 24 hr (Davies, 1974). The pH of the test soil was determined with an appropriately calibrated pH meter (Orion, Model 510) using Method 9045 (U.S. EPA, 1986). Total element and As soil and house dust concentrations were determined using Method 3050 for sample preparation and digestion along with Method 6010 (inductively coupled plasma atomic emission spectroscopy, ICP-AES) and Method 7060 (atomic absorption method) for determination of actual metal concentrations (U.S. EPA, 1986). The As micromineralogy of the composite soil and dust samples was determined by electron microprobe analysis by the method of Davis *et al.* (1993). Particle size analysis of the soil was determined by the electrozone method (Particle Data Laboratories, Ltd., Elmhurst, IL).

Test System and Animal Maintenance

This was a nonclinical laboratory study performed in compliance with the EPA Good Laboratory Practice Regulations, 40 CFR Part 792 (U.S. EPA, 1989). Three female cynomolgus monkeys (approximately 2–3 kg and 3–3½ years of age) were supplied by Charles River Primates (Port Washington, NY) and were housed in stainless-steel metabolism cages for the duration of the study.

All monkeys were provided deionized water (<0.002 μg As/ml) *ad libitum*. Certified Purina Primate Diet 5048 (<0.2 μg As/g) was also available *ad libitum*, except during a fasting period which was initiated approximately 16 hr prior to dosing and concluded approximately 4 hr after dosing.

Dosing Regimen and Administration

Each of the three female monkeys were randomly cycled through the four different treatments, with a washout period of at least 14 days between treatments. The four treatments consisted of a single intravenous or gavage administration (1 ml/kg body wt) of a sodium arsenate solution (0.62 mg As/kg body wt) or a single oral administration via capsules of soil or house dust (1.5 g of soil/kg body wt or 0.62 mg As/kg body wt; 1.5 g of house dust/kg body wt or 0.26 mg As/kg body wt).

For the intravenous treatment, the aqueous sodium arsenate solution was administered over a 2- to 3-min interval into the saphenous vein using a Butterfly Infusion Set (25 × ¾ 12-in. Tubing, Abbott Hospital, Inc., North Chicago, IL) which was Luer-Lok fitted to a disposable syringe.

For the oral sodium arsenate treatment, the aqueous solution was administered over a 1-min interval using a plastic syringe that was fitted with an 8 F (French) rubber gavage tube (Mallinckrodt, Glens Falls, NY). The feeding tube was passed via the nasal passage down the esophagus to the stomach. Dosing solution concentrations were verified during the study and were all within ±2% of target concentrations.

The targeted amount of the test substances (soil or house dust) was formulated into appropriately sized gelatin capsules (Lilly No. 000 or 00) so that the total weight of the soil or dust contained in the set of capsules was within ±5% of the targeted dose. Dosing was performed using a pilligun (Professional Specialties, Inc.), with a 1- to 4-min interval between each capsule administration. Four capsules were required to deliver the target dose of soil or house dust, and the monkeys were monitored to ensure that capsules or test substances were not expelled.

Sample Collection and Preparation

Excreta specimens were collected for each treatment from all monkeys prior to dosing and at the end of the intervals of 0–24, 24–48, 48–72, 72–96, 96–120, 120–144, and 144–168 hr after dosing. Urine flowed into a runoff jar attached to the collection pan of the cage. After the urine and feces specimens were removed, the cages and collection pans were rinsed with deionized water (cage rinse) to remove any residual excreta. All specimens were weighed to the nearest 0.1 g at room temperature. The excreta and cage rinse specimens for the first 120 hr were pooled to provide specimens for analysis at 0–24, 24–72, and 72–120 hr after dosing. Urine and cage rinse samples were acidified with 15 M HNO_3. Deionized water (a volume equivalent to twice the total wet weight of the fecal specimen) was mixed with the pooled fecal specimens on a shaker until a homogenous paste was produced. Splits of fecal material were lyophilized and subject to heavy-liquid separation for determination of As speciation by electron microprobe.

Animals were bled according to the following time points—oral dose (gavage and capsule): predose, 15, 30, 45, 60, and 90 min and 2, 3, 4, 8, 24, 48, 72, 96, 120, 144, and 168 hr postdose; intravenous dose: predose, 2, 5, 10, 15, 30, and 60 min and 2, 4, 8, 24, 48, 72, 96, and 120 hr postdose. A 6-hr blood collection was added to the dust animals. Approximately 1.0 ml of blood was taken from the monkeys at each time point using vascular access ports which had been previously implanted. A 22-gauge × 1-in. Huber point needle (Norfolk Medical Products) attached to a 3-ml syringe was used to withdraw the blood which was then placed into a 10-ml Vacutainer (with sodium heparin, Becton Dickinson, Rutherford, NJ). Heparin was also diluted and used to block the vascular access ports in between bleeds in order to maintain their patency. After collection, 1 ml of each of the blood samples was measured and then added in a 1:5 dilution to 0.2% (v/v) nitric acid and stored at approximately 5°C prior to analysis. The 144- and 168-hr samples for the gavage, dust, and soil animals were not analyzed.

Determination of Arsenic in Biological Fluids

Excreta. All samples were analyzed using a Perkin–Elmer Model 5000 Zeeman atomic absorption spectrophotometer equipped with a Model 500 graphite furnace (GFAA). Fecal specimens (approximately 3 g) were refluxed with 15 M HNO_3 at 95°C and evaporated to 5–10 ml. Samples were then digested with 2 ml of water and approximately 5 ml of 30% H_2O_2 and diluted to 50 ml with water. Urine (0.5 to 1.0 ml) and cage rinse (~ ml) samples were digested in 15 M HNO_3 in a boiling water bath. After cooling, samples were diluted to approximately 5 ml with deionized water.

An As matrix modifier solution was used, consisting of 0.5% Ni (2.5% $Ni(NO_3)_2 \cdot 6H_2O$) and 0.25% magnesium (2.6% $Mg(NO_3)_2 \cdot 6H_2O$) in 1% (v/v) HNO_3 (U.S. EPA, 1983, 1986). In most cases, 20- to 25-μl aliquots of the samples with 5 μl of matrix modifier were injected onto the platform of the graphite furnace and peak-area integration absorbances were measured. Arsenic in the samples was calculated from linear regression equations using the method of standard additions (Klein and Hach, 1977). Arsenic detection limits for the feces, urine, and cage rinse were determined for each treatment cycle and averaged 0.24 μg/g, 0.021 μg/ml, and 0.003 μg/ml, respectively. Prior to further calculations and statistical analysis, the detection limit divided by two was substituted for all As concentrations below the detection limit.

Blood. Blood samples were weighed into acid digestion vessels (Parr Bomb, Model 4749, Parr Instrument Co., Moline, IL) and digested with 5 ml of concentrated nitric acid (Ultrex Brand, J.T. Baker, Inc., Phillipsburg, NJ, ~70% w/w) at 140°C for ~3 hr. After cooling, bomb contents were quantitatively transferred to a volumetric flask and diluted to 10 ml with deionized water.

Samples were analyzed on a Perkin–Elmer Model 5100 atomic absorption spectrophotometer with Zeeman effect background correction (Perkin

Elmer, Norwalk, CT) using the stabilized temperature platform furnace at 193.7 nm using a 10 mg/ml nickel nitrate matrix modifier. Samples were introduced into the graphite furnace atomic absorption spectrophotometer (GFAAS) using a Perkin–Elmer AS-60 autosampler. The spectrophotometer was calibrated against standards prepared in spiked blank blood digests containing As concentrations in the range from 0.05 to 2 μg As/sample using a quadratic least-squares fit of integrated absorbance values (absorbance–seconds) to As concentrations. Sample digests with As concentrations above 2 μg/sample were diluted with blank whole blood digests to produce a final concentration within the GFAAS calibration range.

The limit of detection (LOD) for As in blood (0.007 μg/ml) was calculated as the blank concentration plus three times the standard deviation of the blank.

Calculations

Area under the blood concentration versus time curve (AUC) data were obtained from the Sigma Plot (Version 5.0) program using the trapezoidal rule. In calculating the AUCs, values were corrected for background (predose). If the predose sample was less than the LOD (0.007 μg/ml), then half of the LOD (0.0035) was used and subtracted from all later values through 120 hr. For the intravenous group, the AUCs from $0 \rightarrow \infty$ were estimated using the existing data for each animal and determining the slope of the elimination phase using Lotus 123 (Version 2.3). The equation used was

$$AUC_{0\rightarrow\infty} = AUC \text{ (trapezoidal rule)} + \frac{C_{last}}{slope},$$

where C_{last} is the last measurable concentration.

Due to the design of the study, each monkey served as its own reference. Therefore, bioavailability values based on urinary excretion data for the oral treatments were calculated from the amount of As recovered in the urine when the animal was administered As intravenously compared to uptake of As from the gavage, soil, and dust routes of administration. Bioavailability values based on urine were determined according to the following equation after normalization of the intravenous treatment's arsenic recovery data to 100%.

$$\frac{\text{Total amount of As in urine } (\mu g) \text{ for oral group}}{\text{Total amount of As in urine } (\mu g) \text{ for intravenous group}} \times \frac{\text{Total administered dose for intravenous group (mg/kg)}}{\text{Total administered dose for oral group (mg/kg)}} \times 100.$$

Bioavailability values based on blood were determined according to the following equation.

$$\frac{\text{AUC for oral treatment}}{\text{AUC for intravenous treatment}} \times \frac{\text{Total administered dose for intravenous treatment (mg/kg)}}{\text{Total administered dose for oral treatment (mg/kg)}} \times 100.$$

RESULTS

Soil and House Dust Characterization

Arsenic concentrations in the soil and house dust were 410 and 170 ppm, respectively, with a moisture content of 2.3 and 4.9%, respectively. Percentage organic matter was approximately 3–4 times higher for the house dust than for the soil (42 and 12%, respectively) reflecting the fact that a major component of house dust is exfoliated skin cells and hair. The pH was similar for the soil and house dust (7.8 and 7.6, respectively).

Electron microprobe analysis indicated that the As was present primarily as iron–As oxide (17%-soil, 9%-dust) and combined metal oxides (46%-soil, 58%-dust), with lesser contributions from metal–As silicate, enargite, slag, As phosphate, and iron–As sulfate (Table 1). The metals contained in the metal–As oxide and metal–As silicate were copper, iron, aluminum, and zinc. Although the As mass distributions of the house dust and soil samples were similar, the house dust had more frequent occurrences of liberated As particles (particles not encapsulated or rinded by other mineral forms).

The geometric mean size (GMS) of the soil particles was calculated using volume-based diameter distribution data and was similar for both the soil and house dust (25.2 and 30.8 μm, respectively). These results indicated the particle sizes of the test soil and house dust were consistent with those found to adhere to children's hands (<100 μm) which have a greater likelihood of being ingested (Duggan *et al.*, 1985; Chaney *et al.*, 1989).

In-Life Parameters

There were no treatment-dependent changes in body weight, as the weight of the monkeys remained stable throughout the duration of the study. In addition, no clinical signs of toxicity were observed in any of the animals during the study. Food consumption by one of the monkeys was temporarily reduced after dosing with soil and dust, due to a decrease in the animal's appetite. Otherwise, mean food consumption was similar among the animals throughout the study.

Total Arsenic Amounts and Percentage of Dose in Urine and Feces

Background corrected urine As concentrations for all treatment cycles ranged from <0.021 to 4.68 μg/ml. Each animal's As concentrations during a given treatment cycle were corrected for that animal's background arsenic level, as determined prior to the treatment cycle in question. Peak As excretion in the urine occurred during the collection interval at 0–24 hr for all four treatments (Fig. 1). Arsenic excretion was greatly reduced in subsequent urine samples, indicating that the element was rapidly cleared from the systemic circulation, and that urinary As excretion was virtually complete within 72 hr after dosing. Mean As masses recovered in the urine after 120 hr are provided in Table 2. Low cage rinse values indicate that urine readily drained into the urine collection container, with nominal residual drying on the metabolism cage and/or collection pan. Over 72 hr, approximately 96 and 73% of the total As were recovered in the urine of the intravenous- and gavage-dosed monkeys, respectively, compared to 15 and 26% for the soil and house dust treatments, respectively.

TABLE 1
Arsenic Mass Distribution (%) in Mineral Phases

Phase	Composite soil		Composite house dust	
	Preingested	Postingested	Preingested	Postingested
Metal[a]–arsenic oxide	46	65	58	50
Iron–arsenic oxide	17	15	9	8
Metal[b]–arsenic sulfide	7	5	11	38
Arsenic phosphate	7	8	6	1
Slag	7	5	8	3
Metal[c]–arsenic silicate	11	2	7	1
Iron–arsenic sulfate	5	1	1	0
Number of particles counted	587	179	207	187
Arsenic concentration (mg/kg)	410		170	

[a] Metals in metal–arsenic oxide are primarily copper, zinc, and iron in varying proportions.
[b] Metal–arsenic sulfide is generally a combination of enargite (Cu_3AsS_4), arsenopyrite (FeAsS), and complex solid solutions containing Cu, Te, Pb Bi, or other metals.
[c] Metals in metal–arsenic silicate are primarily iron and aluminum in varying proportions.

Fecal As concentrations ranged from <0.24 to 31.1 μg/g. Typically, fecal As excretion peaked within 24–72 hr of dosing, and As excretion in the feces was generally complete within 72 hr of dosing for all treatment groups (Fig. 2).

Total percentage recoveries of As as a function of the actual administered dose measured in the urine (urine and cage rinse combined) and feces were within 100 ± 6% for the three oral treatments and 80% for the intravenous group (Table 2). Overall, actual administered doses averaged approximately 100% of the targeted administered dose. These results indicated that animals were administered accurate doses of As via the various routes of administration.

Absolute Percentage Bioavailability

Total amounts of As in urine, AUCs, and absolute percentage bioavailability values based on urine and blood data are provided in Table 3.

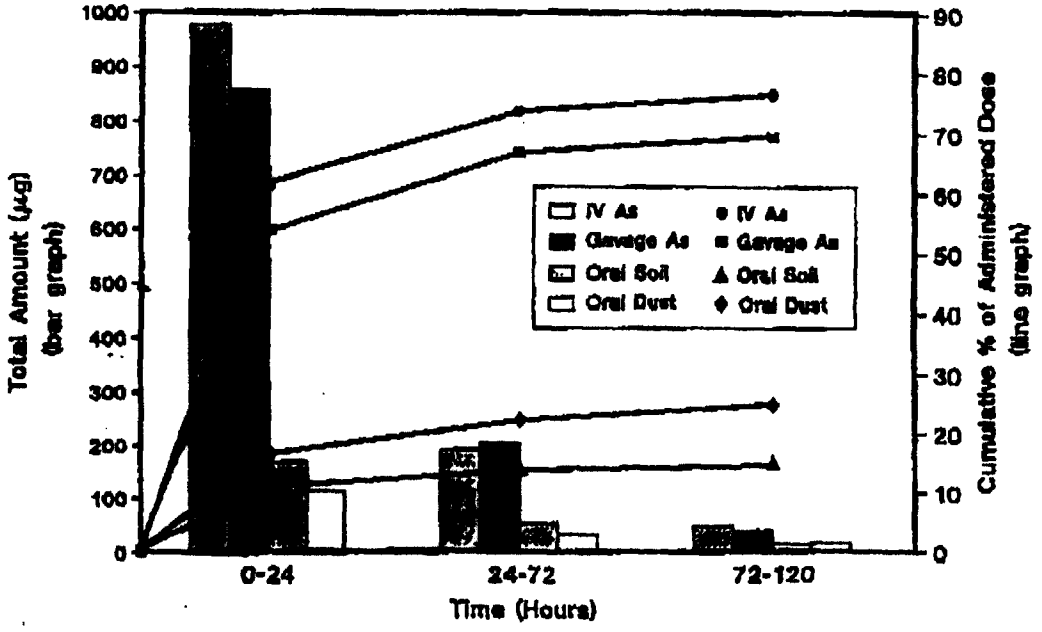

FIG. 1. Arsenic excreted in urine at each time interval (bars) and as cumulative percent of administered dose (lines). Treatment groups of three monkeys were given target doses of 0.62 mg As/kg body wt of sodium arsenate by intravenous or gavage administration, or 1.5 g of soil or house dust per kilogram body wt (0.62 and 0.26 mg As/kg body wt, respectively) by oral administration via capsules.

TABLE 2

Mean Arsenic Mass Recovered in Urine after 5 Days and Percentage Recovery of Administered Arsenic[a]

Treatment group	Arsenic mass administered[b] (μg)	Arsenic mass in urine[c] (μg)	Percentage recovery[d]		
			Urine	Feces	Total
Intravenous sodium arsenate	1593 ± 38	1220 ± 54	76.5 ± 2.5	3.2 ± 1.9	79.7 ± 4.0
Gavage sodium arsenate	1595 ± 47	1105 ± 74	69.2 ± 3.0	25.0 ± 11.3	94.4 ± 9.2
Oral soil	1550 ± 94	238 ± 86	15.2 ± 4.7	86.4 ± 11.1	101 ± 7
Oral dust	656 ± 31	164 ± 28	25.0 ± 3.2	70.5 ± 2.2	95.4 ± 5.2

[a] Treatment groups of three monkeys were given target doses of 0.62 mg As/kg body wt of sodium arsenate administered intravenously or by gavage, or 1.5 g of soil or dust per kilogram body wt (0.62 and 0.26 mg As/kg body wt, respectively) orally via capsules.

[b] Values are means ± standard deviation of total amounts of arsenic administered to each animal ($N = 3$).

[c] Values are means ± standard deviation of total As amounts in urine obtained over 120 hr for each animal ($N = 3$).

[d] Values are means ± standard deviation of percentage recovery values for each animal ($N = 3$).

Blood data for animal 20-784 following gavage administration revealed a lower peak arsenic concentration than the other two monkeys which may account for the lower absolute bioavailability for that animal. The higher AUC and resultant absolute percentage bioavailability for animal 30-544 following administration of house dust was probably a result of higher blood arsenic concentrations achieved for this animal. Finally, the fact that arsenic concentrations for the final two blood collections were much higher for animal 30-537 after soil administration than those for the other two monkeys resulted in higher AUC and absolute percentage bioavailability values.

Mean normalized absolute percentage bioavailability values based on urine were 67.6, 19.2, and 13.8%, respectively, for the gavage, house dust, and soil groups. Corresponding absolute percentage bioavailability values based on blood were 91.3, 9.8, and 10.9%. The arsenic in the dust and soil was approximately 3.5- to 5-fold (based on urine) and 8- to 9-fold (based on blood) less bioavailable than arsenic in solution. The bioavailabilities of dust and soil arsenic relative to dissolved arsenic were 28 and 20% based on urine values. When blood values were used, the bioavailabilities of dust and soil arsenic relative to dissolved arsenic were reduced 61 and 40% to 11 and 12%, respectively.

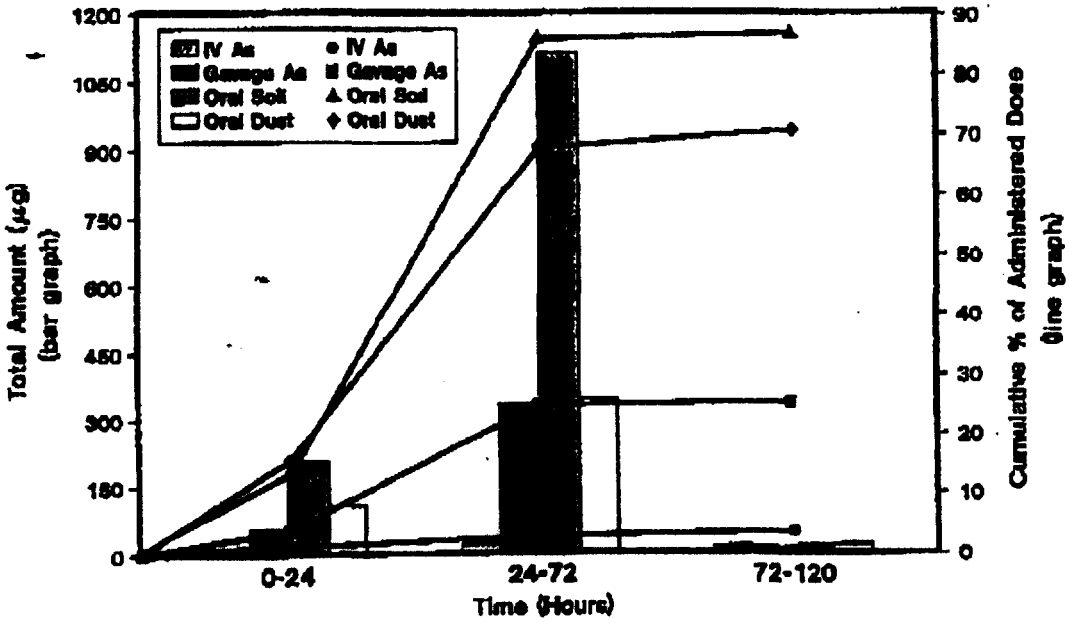

FIG. 2. Arsenic excreted in feces at each time interval (bars) and as cumulative percent of administered dose (lines). Treatment groups of three monkeys were given target doses of 0.62 mg As/kg body wt of sodium arsenate by intravenous or gavage administration, or 1.5 g of soil or house dust per kilogram body wt (0.62 and 0.26 mg As/kg body wt, respectively) by oral administration via capsules.

TABLE 3
Mean Absolute Percentage Bioavailability

Treatment	Animal no.	Dose (mg As/kg body wt)	Actual total amount of arsenic administered (μg)	Based on urine: Background corrected total amount of arsenic in urine (μg)	Based on urine: Normalized[a] absolute bioavailability	Based on urine: Mean[b] normalized absolute bioavailability	AUC	Based on blood: Absolute[c] bioavailability	Based on blood: Mean[b] absolute bioavailability
Intravenous	30–544	0.63	1618	1253			3.18		
	20–784	0.60	1550	1156			4.24		
	30–537	0.64	1612	1146			4.72		
Gavage	30–544	0.61	1643	1138	72.6	67.6 ± 2.6	3.10	100.7	91.3 ± 12.4
	20–784	0.60	1593	993	64.1		2.83	66.7	
	30–537	0.63	1550	1048	66.0		4.95	106.5	
Oral dust	30–544	0.26	687	144	21.5	19.2 ± 1.5	0.24	18.3	9.8 ± 4.3
	20–784	0.26	625	109	16.3		0.08	4.4	
	30–537	0.26	657	129	19.7		0.13	6.8	
Oral soil	30–544	0.58	1658	299	20.1	13.8 ± 3.3	0.20	6.8	10.9 ± 5.2
	20–784	0.62	1491	190	11.9		0.20	4.6	
	30–537	0.62	1501	145	9.3		0.97	21.2	

Note. Each monkey was its own reference and absolute bioavailability was determined for the three oral treatments (gavage, oral soil, and oral dust) using the following equation:

$$\frac{\text{Total amount of As in urine } (\mu g) \text{ for oral treatment}}{\text{Total amount of As in urine } (\mu g) \text{ for intravenous treatment}} \times \frac{\text{Total administered dose for intravenous treatment (mg/kg)}}{\text{Total administered dose for oral treatment (mg/kg)}} \times 100.$$

Bioavailability was determined after normalization of intravenous treatment's arsenic recovery data to 100%. For example, for animal 30–544 (gavage), the bioavailability value calculated from the above equation is then divided by normalization factor $\frac{1643}{1618}$.

[b] Values are mean ± standard error of the mean.

[c] $\frac{\text{Area under the curve (AUC) for oral treatment}}{\text{Area under the curve (AUC) for intravenous treatment}} \times \frac{\text{Total administered dose for intravenous treatment (mg/kg)}}{\text{Total administered dose for oral treatment (mg/kg)}} \times 100.$

DISCUSSION

This study confirmed that in cynomolgus monkeys, as in other species, urinary excretion is the major pathway of As elimination from the systemic circulation (Buchet *et al.*, 1981; Charbonneau *et al.*, 1978; Marafante and Vahter, 1987; Tam *et al.*, 1979; Vahter, 1981; Yamauchi and Yamamura, 1985). For the intravenous treatment, the urinary data indicated that As elimination had essentially ceased within 72 hr of dosing, indicating that the 5-day in-life phase was sufficient to recover most of the absorbed As (Fig. 1). Arsenic recovery in the feces for the intravenous treatment indicated that some As was eliminated by biliary excretion; however, this study could not determine the extent of this As recycling. Urinary As excretion following intravenous administration was normalized to account for the sum of As retained in tissues and eliminated via feces. For the gavage sodium arsenate, soil, and house dust treatments, approximately 25, 86, and 71% of the actual administered As dose was eliminated in the feces, respectively, representing the amount of As that was not absorbed plus the fraction of absorbed As that was eliminated by biliary excretion and not reabsorbed. Assuming that the fraction of As eliminated through biliary excretion was constant, the higher percentage of the administered As dose recovered in the feces of the soil and house dust animals when compared to the gavage treatment indicated that soil- and dust-As were in a less absorbable form than the sodium arsenate and, consequently, less bioavailable.

The almost perfect total As recoveries in the oral groups demonstrated the capability of the protocol used to recover administered As and were not necessarily inconsistent with the 20% tissue retention suggested by the intravenous data. Arsenic recovery data for the intravenous treatment suggested that differences in arsenic distribution and metabolism following a bolus of sodium arsenate administered intravenously compared to orally may affect bioavailability estimates. The rate and extent of distribution of a drug/chemical to various tissues depends upon the rate of delivery of the substance to the tissue circulation (Welling, 1989). Additionally, As metabolism is likely to be affected by the route of administration. Arsenic elimination is enhanced by conversion to methylated species in the liver (McKinney, 1992). Intravenously administered As will circulate through the pulmonary capillary bed and other tissues prior to reaching the liver. These factors suggest that a larger fraction of the absorbed dose is likely to be retained in the tissues after intravenous compared to oral administration. Because of this apparent difference, urinary As excretion following intravenous administration was normalized, whereas urinary As excretion following oral administration was not, to preclude overestimation of As bioavailability.

Urinary excretion time course patterns indicated that these data were acceptable for estimating As bioavailability because virtually all of the As was recovered. The overall absolute percentage bioavailabilities of As in the test soil and house dust based on comparison with normalized intravenous urinary data were 14 and 19%, respectively, suggesting that only a small fraction of the As in the test substances was available for absorption. This was further supported by absolute percentage bioavailabilities based on blood data of 11 and 10%, respectively. Arsenic in the soil and house dust was approximately 3.5- to 5-fold (based on urine) and 8- to 9-fold (based on blood) less bioavailable than arsenic in solution, probably because As in the soil and dust occurred predominantly as As minerals that are generally insoluble during passage through the monkey gastrointestinal tract. Indeed, examination of the As mineralogy in fecal material from the monkeys indicated the presence of all of the As mineral phases present in the initial soil and house dust (Table 1). Based on the As mineralogy in fecal material, the phases metal–As silicate and iron–As sulfate appear to contribute the bulk of bioavailable As.

As arsenic-bearing minerals pass through the gastrointestinal tract, their solubility is controlled by a variety of mineralogic factors including (1) the solubility of the As-bearing phases, (2) encapsulation within insoluble matrices (e.g., silica), (3) rinding of the As grain by precipitation or alteration reactions that occur during weathering and protect the As mineral from dissolution, and (4) dissolution kinetics of the As-bearing minerals (Davis *et al.*, 1992). Arsenic mineralogy of the soil and house dust was nearly identical, suggesting that the two matrices should yield similar As bioavailabilities.

A recent As bioavailability study conducted in dogs has also indicated limited As bioavailability from soil (Groen *et al.*, 1993). Arsenic was administered as an intravenous solution (As_2O_5) or orally as As in soil to groups of six dogs, and urine was collected in 24-hr fractions for 120 hr. After 120 hr, 88 ± 16% of the dose administered intravenously was excreted in the urine, compared to only 7.0 ± 1.5% excreted in the urine after oral soil administration. The calculated bioavailability of inorganic As from soil based on urinary excretion data was 8.3 ± 2.0%, consistent with the data from the present study. Thus, the bioavailability of soil and house dust As relative to dissolved As of between 10 and 30% in the current study along with the results of Groen *et al.* (1993) demonstrate the importance of accurately accounting for differences in the bioavailability of As in different media when assessing potential environmental exposures.

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